

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>45460-PT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/CA 00/01153</b>	International filing date (day/month/year) <b>03/10/2000</b>	(Earliest) Priority Date (day/month/year) <b>04/10/1999</b>
Applicant <b>GAN, Zhibo</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable (See Box I).**

3.  **Unity of invention is lacking (see Box II).**

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.       

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01153

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 G01N33/543 G01N33/542 C12Q1/68 C12Q1/34

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 25665 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 22 August 1996 (1996-08-22) the whole document ---	1-9, 11
Y	---	10, 12-25
X	WO 98 39471 A (TROPIX, INC.) 11 September 1998 (1998-09-11) the whole document ---	12-25
Y	WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999 (1999-07-01) the whole document ---	1-25
Y	WO 96 08721 A (BIOCIRCUITS CORPORATION) 21 March 1996 (1996-03-21) the whole document ---	1-25
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- A\* document defining the general state of the art which is not considered to be of particular relevance
- E\* earlier document but published on or after the international filing date
- L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- O\* document referring to an oral disclosure, use, exhibition or other means
- P\* document published prior to the international filing date but later than the priority date claimed

- T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- &\* document member of the same patent family

Date of the actual completion of the international search

20 February 2001

Date of mailing of the international search report

27/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Griffith, G

## INTERNATIONAL SEARCH REPORT

International Application No

/CA 00/01153

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23) the whole document ---	12-25
Y	EP 0 309 230 A (M.L. TECHNOLOGY VENTURES, L.P) 29 March 1989 (1989-03-29) abstract ---	10
A	WO 90 12888 A (BIOCONTROL SYSTEMS, INCORPORATED) 1 November 1990 (1990-11-01) the whole document ---	1-25
A	EP 0 244 932 A (BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM) 11 November 1987 (1987-11-11) the whole document ----	1-25
A	US 4 391 904 A (D. J. LITMAN ET AL.) 5 July 1983 (1983-07-05) the whole document -----	1-25

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

/CA 00/01153

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9625665	A 22-08-1996	AU 714839 B AU 4982196 A CA 2211972 A EP 0809803 A JP 11500223 T US 6103217 A US 6080423 A		13-01-2000 04-09-1996 22-08-1996 03-12-1997 06-01-1999 15-08-2000 27-06-2000
WO 9839471	A 11-09-1998	AU 6443498 A EP 0972071 A		22-09-1998 19-01-2000
WO 9932655	A 01-07-1999	US 5972595 A AU 2000699 A EP 1042500 A US 6066446 A		26-10-1999 12-07-1999 11-10-2000 23-05-2000
WO 9608721	A 21-03-1996	CA 2199149 A EP 0781413 A JP 10505904 T		21-03-1996 02-07-1997 09-06-1998
WO 9816657	A 23-04-1998	AU 4904397 A		11-05-1998
EP 309230	A 29-03-1989	AT 124143 T AU 633474 B AU 2554188 A CA 1339872 A DE 3854029 D DE 3854029 T DK 244889 A EP 0638807 A ES 2074051 T FI 892435 A JP 2503147 T JP 2000350598 A JP 2000350599 A KR 9602561 B NO 892043 A PT 88562 A, B WO 8902476 A US 5639604 A US 5948899 A US 6004745 A US 5283174 A		15-07-1995 04-02-1993 17-04-1989 19-05-1998 27-07-1995 26-10-1995 20-06-1989 15-02-1995 01-09-1995 19-05-1989 04-10-1990 19-12-2000 19-12-2000 22-02-1996 17-07-1989 31-07-1989 23-03-1989 17-06-1997 07-09-1999 21-12-1999 01-02-1994
WO 9012888	A 01-11-1990	AU 639237 B AU 5655290 A CA 2062753 A DE 69020555 D DE 69020555 T EP 0470172 A JP 3043063 B JP 4504802 T US 5403721 A		22-07-1993 16-11-1990 28-10-1990 03-08-1995 02-11-1995 12-02-1992 22-05-2000 27-08-1992 04-04-1995
EP 244932	A 11-11-1987	US 4859581 A AU 609386 B AU 6987087 A DK 122087 A		22-08-1989 02-05-1991 17-09-1987 04-12-1987

# INTERNATIONAL SEARCH REPORT

## Information on patent family members

International Application No

/CA 00/01153

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 244932	A	FI 871039 A FI 924243 A FI 924244 A NO 870977 A NO 930635 A US 5332812 A JP 62265998 A US 5262403 A	11-09-1987 22-09-1992 22-09-1992 11-09-1987 11-09-1987 26-07-1994 18-11-1987 16-11-1993
US 4391904	A 05-07-1983	US 4299916 A US 5342759 A US 4533629 A US 4540659 A US 5432057 A AU 538687 B AU 6132080 A BR 8007330 A CA 1138332 A DE 3071340 D EP 0032286 A ES 495936 D ES 8202364 A IL 60817 A JP 1030109 B JP 1548194 C JP 61269068 A JP 1465415 C JP 56092218 A JP 63012260 B MX 6798 E US 5156953 A US 4843000 A	10-11-1981 30-08-1994 06-08-1985 10-09-1985 11-07-1995 23-08-1984 02-07-1981 30-06-1981 28-12-1982 20-02-1986 22-07-1981 16-01-1982 16-04-1982 29-02-1984 16-06-1989 09-03-1990 28-11-1986 10-11-1988 25-07-1981 18-03-1988 25-07-1986 20-10-1992 27-06-1989

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GALE, Edwin J. et al.  
KIRBY EADES GALE BAKER  
Box 3432, Station D  
Ottawa, Ontario K1P 6N9  
CANADA

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KEGB

FEB - 4 2002

PCT

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CHECKED \_\_\_\_\_

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year)	23.01.2002
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Applicant's or agent's file reference <b>45460-PT</b>	<b>IMPORTANT NOTIFICATION</b>
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International application No. <b>PCT/CA00/01153</b>	International filing date (day/month/year) <b>03/10/2000</b>	Priority date (day/month/year) <b>04/10/1999</b>
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Applicant <b>GAN, Zhibo</b>
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1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
---------------------------------------	--------------------

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D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 pmu d  
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Authorized officer

Danti, B

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**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
**(PCT Article 36 and Rule 70)**

Applicant's or agent's file reference <b>45460-PT</b>	<b>FOR FURTHER ACTION</b> <small>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</small>																	
International application No. <b>PCT/CA00/01153</b>	International filing date (day/month/year) <b>03/10/2000</b>	Priority date (day/month/year) <b>04/10/1999</b>																
International Patent Classification (IPC) or national classification and IPC <b>G01N33/543</b>																		
Applicant <b>GAN, Zhibo</b>																		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 2 sheets.</p>																		
<p>3. This report contains indications relating to the following items:</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 10%; text-align: right; padding-right: 5px;">I</td> <td style="width: 90%; padding-left: 5px;"><input checked="" type="checkbox"/> Basis of the report</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">II</td> <td style="padding-left: 5px;"><input type="checkbox"/> Priority</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">III</td> <td style="padding-left: 5px;"><input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">IV</td> <td style="padding-left: 5px;"><input type="checkbox"/> Lack of unity of invention</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">V</td> <td style="padding-left: 5px;"><input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">VI</td> <td style="padding-left: 5px;"><input type="checkbox"/> Certain documents cited</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">VII</td> <td style="padding-left: 5px;"><input type="checkbox"/> Certain defects in the international application</td> </tr> <tr> <td style="text-align: right; padding-right: 5px;">VIII</td> <td style="padding-left: 5px;"><input checked="" type="checkbox"/> Certain observations on the international application</td> </tr> </table>			I	<input checked="" type="checkbox"/> Basis of the report	II	<input type="checkbox"/> Priority	III	<input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	IV	<input type="checkbox"/> Lack of unity of invention	V	<input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	VI	<input type="checkbox"/> Certain documents cited	VII	<input type="checkbox"/> Certain defects in the international application	VIII	<input checked="" type="checkbox"/> Certain observations on the international application
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VI	<input type="checkbox"/> Certain documents cited																	
VII	<input type="checkbox"/> Certain defects in the international application																	
VIII	<input checked="" type="checkbox"/> Certain observations on the international application																	

Date of submission of the demand <b>02/05/2001</b>	Date of completion of this report <b>23.01.2002</b>
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  <b>Linker, W</b>  Telephon No. +49 89 2399 8703



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA00/01153

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1,2,4-9 as originally filed

3,3a as received on 20/12/2001 with letter of 14/12/2001

**Claims, No.:**

1-25 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA00/01153

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	1-11, 19-21, 23
	No:	Claims	12-18, 22, 24, 25
Inventive step (IS)	Yes:	Claims	1-11
	No:	Claims	12-25
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

**2. Citations and explanations  
see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**s separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/01153

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999

(1999-07-01)

D2: WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23)

The subject-matter of present claims 12-15 and 24 is already known from document D1, see in particular page 3, lines 6-15, 21 and 24, page 5, lines 5, 15-17 and 23, page 6, lines 1, 8, and 14-24, page 7, lines 1-7 and 12-14. Furthermore, the subject-matter of claims 12-18, 22, 24 and 25 is already known from document D2, see in particular page 2, lines 10-20, page 6, lines 14-16 and 18, page 7, line 6, page 8, line 10 and 14, page 9, lines 3-7. Thus, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 12-18, 22, 24 and 25 is not novel (or inventive according to Article 33(3) PCT).

While the applicant's observations have been considered, the previously expressed opinion is nevertheless maintained for the following reason:

The Applicant has pointed to differences between the prior art and the present invention, however, the wording of the aforementioned claims is such that the claimed subject-matter cannot be distinguished from the above state of the art.

Using respective substrates for the enzymes selected according to dependent claims 19-21 and 23 is not considered to involve an inventive step as the skilled person could expect that the method of D2 can also be applied to enzyme/substrate combinations different from those explicitly mentioned in D2.

The subject-matter of claims 1-11 appears not to be disclosed or suggested by any of the cited prior art documents, thus, the subject-matter of claims 1-11 appears to satisfy the criterions set forth in Article 33(2) and (3) PCT.

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET**

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**R Item VIII**

**Certain observations on the international application**

The features mentioned on page 3, lines 22-24 (i.e. due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction) and page 4, lines 3-4 (i.e. without an additional step) appear to be essential to the claimed method in view of the object indicated on page 3, lines 4-5. Thus, claims 1, 12 and 25 do not satisfy the criterion set forth in Article 6 PCT.

catalytic activity of an enzyme and not just the amount of the enzyme as a given amount of the enzyme may have a widely varying activity depending on reaction conditions.

International PCT Application No. WO 99/32655 filed in the name of Nen

5 Life Science Products, Inc. of Boston, Massachusetts, USA, published on July 1<sup>st</sup>, 1999, relates to a method for analyzing a sample for the presence and/or activity of an enzyme. The invention makes use of a hydrophobic layer formed on a solid support; the hydrophobic layer incorporating by hydrophobic interactions and amphipathic enzyme substrate labeled with a reporter on its hydrophilic

10 region. The hydrophobic material having the substrate disposed therein is contacted with a sample and with a polar solvent, whereby enzyme present in the sample cleaves the substrate and produces a labeled hydrophilic fragment, which fragment migrates to the polar solvent. The presence of the reporter is then detected in the polar solvent or in the hydrophobic layer.

15 International PCT Application No. WO 98/16657 filed in the name of Chiron Corporation of Emeryville, California, USA, which was published on April 23<sup>rd</sup>, 1998, relates to a method of screening a compound capable of regulating protease activity by incubating a protease and a polypeptide in the presence and absence of a test compound. The polypeptide comprises an anchor

20 region, a protease recognition site and a detectable signal region. The anchor region is bound to a solid support and the protease recognition site comprises (a) a protease cleavable peptide bond, and (b) at least three naturally adjacent amino acids on each side of the cleavable peptide bond. The signal region bound to the solid support is detected. Detecting an amount of the signal region bound to the

25 solid support in the presence of the test compound, which is greater or smaller than an amount detected in the absence of the test compound, indicates that the test compound is capable of regulating protease activity.

It is important for developing a method to reduce the step of the measurement procedure.

3 a

## DISCLOSURE OF THE INVENTION

This present invention is for a method referred to as non-separation heterogeneous assay that greatly simplifies the detection, identification, 5 measurement of concentration and activity of biological substances. It is based on the change of the label signal due to the distribution of the label between a solid surface and liquid in a vessel after completion of the reaction among reactants. The method involves the coating of a reactant (labeled or unlabeled) onto a surface, addition of a sample with or without a competitor labeled using a label 10 tag or unlabelled. The change of the label signal can be directly measured.

## DETAILED DESCRIPTION OF THE INVENTION

15 The present invention relates to a new method for the detection, identification, measurement of concentration and activity of biological substances, which is based on the change of the label signal due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction among reactants.

20 1. An assay in which the surface of a vessel is coated with reactant 1 which is a binding ligand for reactant 3 being the labeled form of reactant 2. Competitive binding reactions between reactant 2 and reactant 3 for reactant 1 or between reactant

## PATENT COOPERATION TREATY

REC'D 28 JAN 2002

PCT

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>45460-PT</b>	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. <b>PCT/CA00/01153</b>	International filing date (day/month/year) <b>03/10/2000</b>	Priority date (day/month/year) <b>04/10/1999</b>	
International Patent Classification (IPC) or national classification and IPC <b>G01N33/543</b>			
Applicant <b>GAN, Zhibo</b>			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand <b>02/05/2001</b>	Date of completion of this report <b>23.01.2002</b>
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  <b>Linker, W</b> Telephone No. +49 89 2399 8703



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA00/01153

**I. Basis of the report**

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**Description, pages:**

1,2,4-9 as originally filed

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**Claims, No.:**

1-25 as originally filed

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- the description, pages:
- the claims, Nos.:
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**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CA00/01153

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-11, 19-21, 23
	No:	Claims	12-18, 22, 24, 25
Inventive step (IS)	Yes:	Claims	1-11
	No:	Claims	12-25

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**R Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: WO 99 32655 A (NEN LIFE SCIENCE PRODUCTS, INC.) 1 July 1999  
(1999-07-01)

D2: WO 98 16657 A (CHIRON CORPORATION) 23 April 1998 (1998-04-23)

The subject-matter of present claims 12-15 and 24 is already known from document D1, see in particular page 3, lines 6-15, 21 and 24, page 5, lines 5, 15-17 and 23, page 6, lines 1, 8, and 14-24, page 7, lines 1-7 and 12-14. Furthermore, the subject-matter of claims 12-18, 22, 24 and 25 is already known from document D2, see in particular page 2, lines 10-20, page 6, lines 14-16 and 18, page 7, line 6, page 8, line 10 and 14, page 9, lines 3-7. Thus, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 12-18, 22, 24 and 25 is not novel (or inventive according to Article 33(3) PCT).

While the applicant's observations have been considered, the previously expressed opinion is nevertheless maintained for the following reason:

The Applicant has pointed to differences between the prior art and the present invention, however, the wording of the aforementioned claims is such that the claimed subject-matter cannot be distinguished from the above state of the art.

Using respective substrates for the enzymes selected according to dependent claims 19-21 and 23 is not considered to involve an inventive step as the skilled person could expect that the method of D2 can also be applied to enzyme/substrate combinations different from those explicitly mentioned in D2.

The subject-matter of claims 1-11 appears not to be disclosed or suggested by any of the cited prior art documents, thus, the subject-matter of claims 1-11 appears to satisfy the criterions set forth in Article 33(2) and (3) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/01153

**Re It m VIII**

**Certain observations on the international application**

The features mentioned on page 3, lines 22-24 (i.e. due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction) and page 4, lines 3-4 (i.e. without an additional step) appear to be essential to the claimed method in view of the object indicated on page 3, lines 4-5. Thus, claims 1, 12 and 25 do not satisfy the criterion set forth in Article 6 PCT.

catalytic activity of an enzyme and not just the amount of the enzyme as a given amount of the enzyme may have a widely varying activity depending on reaction conditions.

It is important for developing a method to reduce the step of the measurement 5 procedure.

#### DISCLOSURE OF THE INVENTION

This present invention is for a method referred to as non-separation 10 heterogenous assay that greatly simplifies the detection, identification, measurement of concentration and activity of biological substances. It is based on the change of the label signal due to the distribution of the label between a solid surface and liquid in a vessel after completion of the reaction among reactants. The method involves the coating of a reactant (labeled or unlabeled) onto a surface, addition of a sample with 15 or without a competitor labeled using a label tag or unlabeled. The change of the label signal can be directly measured.

#### DETAILED DESCRIPTION OF THE INVENTION

20 The present invention relates to a new method for the detection, identification, measurement of concentration and activity of biological substances, which is based on the change of the label signal due to the uneven distribution of the label between surface and liquid in a vessel after completion of the reaction among reactants.

25 1. An assay in which the surface of a vessel is coated with reactant 1 which is a binding ligand for reactant 3 being the labeled form of reactant 2. Competitive binding reactions between reactant 2 and reactant 3 for reactant 1 or between reactant